Abstract

We discuss the studies of complex chemical reactions using manual and automated methods in this thesis. When there is sufficient knowledge about the reactants, products and a few intermediates in a reaction, we have modelled the reaction *manually* by sketching the scheme of reactions and guessing the geometries of the stationary points and transition states. This manual modelling was used for the reactions involving multiple spin states or multiple surfaces (in photochemical reactions). For studying reactions with many pathways or unknown products, we developed and used an automated reaction finding method.

In **Chapter 1** a brief history of the developments in understanding chemical reactions are discussed. Some of the recent development in modelling chemcial reactions by manual and automated methods are discussed at the end. A brief background of the basics of quantum chemistry, ab initio and density functional theory, and algorithms for optimization of minimum energy path and stationary points are given.

Enzymatic reactions involving Cytochrome P450 undergoes a multi-state reactivity. In **Chapter 2** we discuss the formation of D-ring in the biosynthesis of anti-cancer drug Taxol. A cluster model containing the active site was used. A new pathway is proposed that is more favorable compared to the previously proposed pathways.

Chapter 3 deals with another set of complex reactions that involve photochemically excited states: a) the excited state intramolecular proton transfer (ESIPT) process through the first singlet excited state (S_1), and, b) the reaction mechanism of photodissociation involved in the removal of photo removable protecting groups through thefirst triplet excited state (T_1).

The development of an improved automated reaction finding method is discussed in **Chapter 4**. A Tabu-search based algorithm is used for improving the search space. The implementation wass validated using a set of Diels-Alder reactions and then applied to the functionalization of graphene.

An application of our automated reaction finding strategy on a challenging problem in pre-biotic chemistry is discussed in **Chapter 5**. We studied the tetramerization of the HCN molecule which is proposed as one of the pathways in the chemical evolution. We have mapped new as well as already discovered reaction routes for the formation of important molecules, DAMN and AICN, in the prebiotic chemistry.

Keywords: Automated reaction finding, Photo-dissociation, Prebiotic Chemistry, Excited state intramolecular proton transfer, Oxetane formation, enzyme catalysis.